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10/589,505	03/08/2007	Emmanuel Lemichez	0510-1145	8380

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EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,505	LEMICHEZ ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/6/09&4/7/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-10 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-10 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Acknowledgment and entry of the Amendment and Supplemental Amendment submitted on 4/6/09 and 4/7/09, respectively, is made. Claims 1-4, 8-10 and 15 are currently pending.

Claim Rejections - 35 USC § 112-2nd paragraph

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4, 8-10, and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it is unclear what is encompassed by the term "Rho GTPase activator belonging to the families of DNT and CNF1". The abbreviations 'DNT' and 'CNF1' should be spelled out the first time they appear in the claims as it is unclear what is encompassed by this terminology. The mere recitation of a name to describe the invention is not sufficient to satisfy the Statute's requirement of adequately describing and setting forth the inventive concept. The claim should provide any structural properties, such as the amino acid sequence of the protein or molecular weight, which would allow for one to identify the protein without ambiguity. The mere recitation of a name does not adequately define the claimed protein. While the specification can be used to provide definitive support, the claims are not read in a

vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed. Applicants have argue that 'protein family' encompasses prteoins which descend from a common ancestor and have similar functions, and significant sequence similarity. This has been fully and carefully considered but is not deemed persuasive. The structure of these proteins cannot be readily elucidated and it is unclear what specific structure is encompassed for patentability purposes. The definition 'similar functions' and 'signficant sequence similarity' are vague themselves and it is unclear what percentage of similarity is encompassed in these terms and what is alike enough to be considered a 'similar function'. The claim remains vague and indefinite. Appropriate correction and/or clarification is required.

Claim 4 is vague and confusing because it is unclear whether the sequences recited in parts (i)-(ii) are fused together or formed in another hybrid manner. Are all of the sequences in part (i) fused together in the order recited or does the protein comprise one or more of these sequences? Additionally, are all of the amino acid sequences recited in part (ii) included in the composition and are they fused to the end of the last sequence in part (i). The wording of the claim is vague and indefinite. Clarification and/or appropriate correction is required.

Claim 15 is vague and indefinite because they it is drawn to a method for 'preparing a composition adding'. It appears the word 'comprising' should follow the word 'composition' Appropriate correction is required.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the method for preparing the 'composition' does not include the 'antigen' as recited in claims 1-4. The current calims are confusing because it is unclear that they are intended to prepare the composition of claim 1 or a new composition of just the immunoadjuvant and excipient. If it is the latter, the claim is drawn to a new invention and will be withdrawn as an 'election by original presentation' as it is no longer drawn to preparing the composition (product) of claims 1-4. Clarification and/or correction is requested..

Claim Rejections - 35 USC § 112-Enablement

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-4, 8-10 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working

examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

Claim 1 is broadly drawn to a vaccine comprising an immunoadjuvant compound which consists of ***any*** Rho GTPase activator which belongs to the protein families of DNT and CNF1 and an antigen and methods for preparing compositions comprising them by adding an excipient. Claims 2-4, 8-10 and 15 recite the polypeptide sequences of specific Rho GTPase activators.

The instant specification does not enable the use of any Rho Gtpase as an immunoadjuvant in a vaccine composition. The structure of Rho Gtpase and their sources vary greatly. It is unclear that they possess a mutual level of adjuvant-like activity. The instant specification has shown unexpected results with the use of cytotoxic necrotizing factor 1 (cnf1) (SEQ ID NO: 2) as an immunoadjuvant and have demonstrated that when the catalytic domain of cnf1 is present and active the polypeptide works to effectively boost the immune response to OVA. It was shown that a catalytically inactive CNF1 mutant did not possess the same adjuvant activity. The specification also has provided a smaller scale example of some success with the use of dermonectrotic toxin (DNT) (SEQ ID NO: 4). However, there are no other examples demonstrating immunoadjuvant activity of any other Rho Gtpase activator. While Applicants need not disclose every single species of a Genus or show working examples for every possible species, a representative number of examples should be shown. Given the great diversity and source of a 'Rho Gtpase' as defined by the instant specification, the examples provided with cnf1 and DNT are insufficient to enable the

broad scope of the invention. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." Additionally, the claims are drawn to 'vaccine compositions' and encompass vaccines drawn to protecting against HIV viruses (see claim 8). There is no known working vaccine to prevent against HIV. The current prevention protocol for HIV is condom use, not sharing IV needles and/or abstinence. There is no known vaccine for HIV. Accordingly, one skilled in the art could not use any HIV antigen and any Rho Gtpase activator and come up with an effective vaccine composition against HIV/AIDS without undue experimentation.

Response to Arguments:

Applicants have argued that it is not the structure of the Rho GTPase activators that are responsible for the immunoadjuvant activity, e.g., DNT and CF1 have low seqeunce identity but can serve as immunoadjuvants. They cite that only the catalytic domain of DNT is sufficient to stimulate sequence OVA immune response in mice and

that the inactivated mutant differs from native CNF1 in virtue of a single amino acid mutation and has not immunoadjuvant activity even though its tertiary structure is identical to CNF1. These arguments have been fully and carefully considered but are not deemed persuasive. The structure of Rho Gtpase and their sources vary greatly. It is unclear that they possess a mutual level of adjuvant-like activity. The instant specification has shown unexpected results with the use of cytotoxic necrotizing factor 1 (cnf1) (SEQ ID NO: 2) as an immunoadjuvant and have demonstrated that when the catalytic domain of cnf1 is present and active the polypeptide works to effectively boost the immune response to OVA. It was shown that a catalytically inactive CNF1 mutant did not possess the same adjuvant activity. The specification also has provided a smaller scale example of some success with the use of dermonectrotic toxin (DNT) (SEQ ID NO: 4). However, there are no other examples demonstrating immunoadjuvant activity of any other Rho Gtpase activator. While Applicants need not disclose every single species of a Genus or show working examples for every possible species, a representative number of examples should be shown. Given the great diversity and source of a 'Rho Gtpase' as defined by the instant specification, the examples provided with cnf1 and DNT are insufficient to enable the broad scope of the invention and the claims should be limited to the specific working embodiments as outlined in the instant specification. . Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context

of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention."

Applicants argue that the aim of the invention is to provide immunoadjuvants and not new antigens and argue that despite that there are not commercially available HIV vaccines, many scientific publications describe them. An appendix is enclosed; however it is noted that these references have not been entered on a PTO-1449 form. The arguments by Applicants have been fully and carefully considered but are not deemed persuasive since the claims, and particularly claim 8 and 15, are drawn to vaccines compositions, not merely immunodjuvants. The vaccine composition comprising HIV antigens requires protection against disease and are not enabled.

Claim Rejections - 35 USC § 112-New Matter&Written Description

4. Claim 1 and 8-10 and 15 (as they depend from claim 1) are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim has been amended to recite the new limitation wherein said immunoadjuvant compound consists of a Rho GTPase activator "belonging to the

protein families of DNT and CNF1". Written support could not be found for this new limitation. Applicant must point to specific support by page and line number or remove it from the claim. The amendment of 4/6/09 does not cite support for this limitation and a review of the specification did not reveal its source.

In 1999, the United States Patent and Trademark Office ("USPTO") published training materials regarding the examination of patent applications under the written description requirement of 35 U.S.C. § 112, first paragraph. (See http ://www.uspto. gov/web/offices/pac/writtende sc.pdf). Since that time, the case law and technology have developed in such a way as to necessitate a revision of the 1999 training materials. Consequently, this 2008 revision was created to supersede and replace the 1999 training materials. To the extent that any conflict exists between the 1999 training materials and the present materials, the present materials control. The claims have been evaluated with regard to written description based on the Written Description Guidelines and Training Materials published in 2008/

The instant claims are drawn to a "A vaccine composition comprising (a) an antigen and (b) an immunoadjuvant compound, wherein said immunoadjuvant compound consists of a Rho GTPase activator belonging to the protein families of DNT and CNF1". What is the structure of this Rho GTPase activator. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a

particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. Applicants have not described the genus of claimed proteins such that the specification might reasonably convey to the skilled artisan that Applicants had possession of the claimed invention at the time the application was filed. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991).

Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "'Written Description" Requirement (66 FR 1099-1111, January 5,2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention

was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed. The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus'" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus.

There are no drawings or structural formulas disclosed of any of these claimed Rho Gtpase activators. There is no art-recognized correlation, e.g., conserved amino sequence, and recited activity. There is some general teaching in the art that some amino acid variations are tolerated without losing a protein's tertiary structure, but conservation of structure in not a surrogate for conservation of function. There is no

teaching in the specification regarding which of the structure can be varied and still produce a polypeptide which has immunoadjuvant activity. Based on the lack of knowledge and predictability in the art, those of ordinary skill in the art would not conclude that the applicant was in possession of the claimed genus of peptides based on disclosure of the single species of only the exact SEQ ID NOS: 1-4 of the peptides.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to Rho Gtpase activators belonging to the protein families of DNT and CF1; 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). With regard to (4) the nature of the invention and (5) the state of the prior art, these have been discussed above. There is no art-recognized correlation, e.g., conserved amino sequence, and recited activity. There is some general teaching in the art that some amino acid variations are tolerated without losing a protein's tertiary structure, but conservation of structure in not necessarily a surrogate for conservation of function. One of skill in the

art would require guidance, in order to make or use the immunoadjuvants in the methods and compositions as instantly claimed.

102(b) rejections withdrawn in view of the amendments to the claims:

5. All of the rejections made under 35 USC 102 in the previous Office Action have been obviated in view of Applicants' amendments to the claims. The documents cited in the previous Office Action describe either structural studies of Rho GTPase activators or genomic studies of bacteria having Rho GTPase activators. None of these documents describe vaccine composition resulting from the specific combination of (i) **an antigen and** (ii) a RhoGTPase activator as an immunoadjuvant. None of these cited documents deal with vaccination and, thus, fail to suggest that Rho GTPase activator has immunoadjuvant properties. Applicants unexpectedly found that these regulatory proteins contained immunoadjuvant-like properties.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645

6/8/09